UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/388,090	08/31/1999	W. JAMES JACKSON	7969-082	3379

7590 06/20/2002

PENNIE & EDMONDS LLP
1155 AVENUE OF THE AMERICAS
NEW YORK, NY 100362711

EXAMINER
DEVI, SARVAMANGALA J N

ART UNIT	PAPER NUMBER
1645	23

DATE MAILED: 06/20/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/388,090	Jackson et al.
Examiner	**Art Unit**
S. Devi, Ph.D.	1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Feb 25, 2002* .

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *37-39 and 48-55* is/are pending in the application.

4a) Of the above, claim(s) *53* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *37-39, 48-52, 54, and 55* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☒ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *21 & 22*
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Request for Continued Examination

1) A request for continued examination under 37 C.F.R 1.114, including the fee set forth in 37 C.F.R 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 C.F.R 1.114, and the fee set forth in 37 C.F.R 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 C.F.R 1.114. Applicants' submission filed on 02/25/02 (paper no. 20) has been entered.

Applicants' Amendment

2) Acknowledgment is made of Applicants' amendment filed 10/23/01 (paper no. 17) in response to the Office Action mailed 05/17/2001 (paper no. 13). With this, Applicants have amended the specification.

Status of Claims

3) Claims 1-36 and 40-47 have been canceled via the amendment filed 09/25/99.

Claims 37-39 have been amended via the amendment filed 10/23/01. It is noted that the clean and marked-up copies of the amended claim 39 are non-identical with regard to the recitation of the concentration of NaCl. Applicants should avoid this sort of discrepancy in future in order to prevent issuance of Notice of non-compliant Amendment under with 37 CFR 1.121.

New claims 54 and 55 have been added.

Claims 37-39 and 48-55 are pending.

Claims 37-39, 48-52, 54 and 55 are under examination.

Information Disclosure Statements

4) Acknowledgment is made of Applicants' Information Disclosure Statements (IDS) filed 11/21/01, 02/25/02 and 05/08/02 (paper no. 14, 21 and 22). The information referred to therein has been considered and a signed copy of the same is attached to this Office Action (paper no. 23). The IDS attached to paper no. 14 and 21 are duplicates and one has been considered.

Objection(s) Maintained

5) The objection to the drawings made in paragraph 7 of the Office Action mailed 12/11/2000 (paper no. 11) is maintained for reasons set forth therein. Applicants state that they have submitted

a photocopy of the formal drawings "to be" submitted upon allowance. However, no such photocopies are of record currently. Applicants are asked to note the changes effected 03 May 2001, particularly the changes to the 'Timing of Corrections':

INFORMATION ON HOW TO EFFECT DRAWING CHANGES

A. Correction of Informalities -- 37 CFR 1.85; 1097 O.G. 36

New formal drawings must be filed with the changes incorporated therein. The art unit number, application number (including series code) and number of drawing sheets should be written on the reverse side of the drawings. Applicant may delay filing of the new drawings until receipt of the "Notice of Allowability" (PTOL-37 or PTO-37). If delayed, the new drawings MUST be filed within the THREE MONTH shortened statutory period set for reply in the "Notice of Allowability" to avoid extension of time fees. Extensions of time may be obtained under the provisions of 37 C.F.R 1.136(a) for filing the corrected drawings (but not for payment of the issue fee). The drawings should be filed as a separate paper with a transmittal letter addressed to the Official Draftsperson.

B. Corrections other than Informalities Noted by Draftsperson on form PTO-948.

All changes to the drawings, other than informalities noted by the Draftsperson, MUST be made in the same manner as above except that, normally, a highlighted (preferably red ink) sketch of the changes to be incorporated into the new drawings MUST be approved by the examiner before the application will be allowed. No changes will be permitted to be made, other than correction of informalities, unless the examiner has approved the proposed changes.

Timing of Corrections

Applicant is required to submit acceptable corrected drawings within the three month shortened statutory period set in the "Notice of Allowability" (PTO-37). Within that three month period, two weeks should be allowed for review of the new drawings by the Office. If a correction is determined to be unacceptable by the Office, Applicant must arrange to have an acceptable correction re-submitted within the original three month period to avoid

the necessity of obtaining an extension of time with extension fees. Therefore, applicant should file corrected drawings as soon as possible.

Failure to take corrective action within the set (or extended) period will result in ABANDONMENT of the application.

Objection(s) Withdrawn

6) The objection to the specification made in paragraph 8(a) of the Office Action mailed 12/11/2000 (paper no. 11) and maintained in paragraph 9 of the Office Action mailed 05/17/01 (paper no. 13) is withdrawn in light of Applicants' amendments to the specification.

Specification - Informalities

7) The specification is objected to for the following reason(s):

(a) The amendment introduced via the inclusion of brackets "[% identity ..... 100, alignment]" to page 3 beginning at line 9 is objected to. The use of brackets [..] indicates deletion as opposed to an amendment. Applicants should correct this to avoid deletion of the words within the brackets during the printing process, since the printer would not retain words within brackets.

(b) The use of the trademarks in the instant specification has been noted in this application. For example, see page 42, line 11: "IsoVitale"; page 47, line 10: "Sepharose"; and page 46, last line: "Centricon-30". Although the use of trademarks is permissible in patent applications, the propriety nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks. It is suggested that Applicants examine the whole specification to make similar corrections to the trademarks, wherever trademark recitations appear.

(c) Applicants' attempt to incorporate subject matter into this application by reference to the DegP amino acid sequence information from GeneBank in the paragraph bridging pages 41 and 42 is improper. The sequence information being improperly incorporated is critical or essential to the practice of the instant invention.

(d) The last paragraph on page 3 of the instant specification refers to a co-pending application by Attorney Docket number as opposed to an application serial number. Correction is requested.

Rejection(s) Withdrawn

8) The rejection of claim 37 made in paragraph 18(a) of the Office Action mailed 05/17/01 (paper no. 13) under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendments to the claims and/or the base claim.

9) The rejection of claims 50-52, which depend from claim 37, made in paragraph 18(b) of the Office Action mailed 05/17/01 (paper no. 13) under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the base claim.

10) The rejection of claim 39 made in paragraph 19 of the Office Action mailed 05/17/01 (paper no. 13) under 35 U.S.C. 112, first paragraph, as being non-enabled, is withdrawn in light of Applicants' amendment to the claim.

11) The rejection of claims 37 and 50-52 made in paragraph 21 of the Office Action mailed 05/17/01 (paper no. 13) under 35 U.S.C § 102(e) as being anticipated by Gilbert *et al.* (US 6,096,529, filed 06/10/1996), is withdrawn in light of Applicants' amendment to the base claim.

12) The rejection of claim 48 made in paragraph 22 of the Office Action mailed 05/17/01 (paper no. 13) under 35 U.S.C § 102(b) as being anticipated by Zheng *et al.* (*Genetics* 143: 941-952, June 1996), is withdrawn.

Rejection(s) Maintained

13) The rejection of claim 39 made in paragraph 18(a) of the Office Action mailed 05/17/01 (paper no. 13) under 35 U.S.C § 112, second paragraph, as being indefinite, is maintained for reasons set forth therein.

14) The rejection of claims 50-52, which depend from claim 39, made in paragraph 18(b) of the Office Action mailed 05/17/01 (paper no. 13) under 35 U.S.C § 112, second paragraph, as being indefinite, is maintained for reasons set forth therein.

Rejection(s) under 35 U.S.C. § 112, First Paragraph

15) Claims 39 and 50-52 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Instant claim currently includes the limitation of "/0.25 mM NaCl/" (see line 5 of the claim). However, there appears to be no descriptive support in the instant specification for this newly added limitation. The descriptive support on page 25, lines 7, is for --0.25M NaCl--, but not for 0.25 'mM' NaCl.

The new limitation in the claim is therefore considered to be new matter. *In re Rasmussen*, 650 F2d 1212 (CCPA, 1981). New matter includes not only the addition of wholly unsupported subject matter but also, adding specific percentages or compounds after a broader original disclosure, or even omission of a step from a method. See M.P.E.P 608.04 to 608.04(c).

Applicants are respectfully requested to point to the descriptive support in the specification as filed, for the newly added limitation, or to remove the new matter from the claim.

16) Claim 55 is rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

New claim 55 recites that the "polypeptide has a serine protease motif". Applicants point to the specification at page 41, line 26 through page 42, line 2 and state that support for this recitation is found in this part of the specification. However, there is no descriptive support in this part of the specification for an NGSP polypeptide which "has a serine protease motif". Therefore, the above-identified new limitation in the claim is considered to be new matter. *In re Rasmussen*, 650 F2d 1212 (CCPA, 1981). New matter includes not only the addition of wholly unsupported subject matter but also, adding specific percentages or compounds after a broader original disclosure, or even omission of a step from a method. See M.P.E.P 608.04 to 608.04(c).

Applicants are respectfully requested to point to the descriptive support in the specification as filed, for the newly added limitation(s), or to remove the new matter from the claim(s).

Rejection(s) under 35 U.S.C § 112, First Paragraph / 101, Utility

17) The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

35 U.S.C. § 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Utility definitions as provided in the REVISED INTERIM UTILITY GUIDELINES TRAINING MATERIALS are reproduced from http://www.uspto.gov/web/menu/utility.pdf.

"Credible Utility" - Where an Applicant has specifically asserted that an invention has a particular "Credible Utility" - Where an Applicant has specifically asserted that an invention has a particular utility, that assertion cannot simply be dismissed by Office personnel as being "wrong". Rather, Office personnel must determine if the assertion of utility is credible (i.e., whether the assertion of utility is believable to a person of ordinary skill in the art based on the totality of evidence and reasoning provided). An assertion is credible unless (A) the logic underlying the assertion is seriously flawed, or (B) the facts upon which the assertion is based is inconsistent with the logic underlying the assertion. Credibility as used in this context refers to the reliability of the statement based on the logic and facts that are offered by the Applicant to support the assertion of utility. A *credible* utility is assessed from the standpoint of whether a person of ordinary skill in the art would accept that the recited or disclosed invention is currently available for such use. For example, no perpetual motion machines would be considered to be currently available. However, nucleic acids could be used as probes, chromosome markers, or forensic or diagnostic markers. Therefore, the credibility of such an assertion would not be questioned, although such a use might fail the *specific* and *substantial* tests (see below).

"Specific Utility" - A utility that is *specific* to the subject matter claimed. This contrasts with a *general* utility that would be applicable to the broad class of the invention. For example, a claim to a polynucleotide whose use is disclosed simply as a "gene probe" or "chromosome marker" would not be considered to be *specific* in the absence of a disclosure of a specific DNA target. Similarly, a general statement of diagnostic utility, such as diagnosing an unspecified disease, would ordinarily be insufficient, absent a disclosure of what condition can be diagnosed.

"Substantial Utility" - A utility that defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities. For example, both a therapeutic method of treating a known or newly discovered disease and an assay method for identifying compounds that themselves have a "substantial utility" define a "real world" context of use. An assay that measures the presence of a material which has a stated correlation to a predisposition to the onset of a particular disease condition would also define a "real world" context of use in identifying potential candidates for preventing measures or further monitoring. On the other hand, the following are examples of situations that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use and, therefore, do not define "substantial utilities":

(A) Basic research, such as, studying the properties of the claimed product itself or the mechanisms in which the material is involved.

(B) A method of treating an unspecified disease or condition. (Note, this is in contrast to the general rule that treatments of specific diseases or conditions meet the criteria of 35 U.S.C § 101.)

(C) A method of assaying for or identifying a material that itself has no "specific and/or substantial utility".

(D) A method of making a material that itself has no specific, substantial and credible utility.

(E) A claim to an intermediate product for use in making a final product that has no specific, substantial and credible utility.

Note that "throw away" utilities does not meet the tests for a *specific* or *substantial* utility. For example, using transgenic mice as snake food is a utility that is neither specific (all mice could function as snake food) nor substantial (using a mouse context of use). Similarly, use of any protein as an animal food supplement or a shampoo ingredient are "throw away" utilities that would not pass muster as specific or substantial utilities under 35 U.S.C § 101. This analysis should, of course, be tempered by consideration of the context and nature of the invention. For example, if a transgenic

mouse was generated with the specific provision of an enhanced nutrient profile, and disclosed for use as an animal food, then the test for specific and substantial *asserted* utility would be considered to be met.

"Well established Utility" - A specific, substantial and credible utility which is well known, immediately apparent, or implied by the specification's disclosure of the properties of a material, alone or taken with the knowledge of one skilled in the art. "Well established utility" does not encompass any "throw away" utility that one can dream up for an invention or a nonspecific utility that would apply to virtually every member of a general class of materials, such as, protein or DNA. If this is the case, any product or apparatus, including perpetual motion machines, would have a well established utility" as landfill, an amusement device, a toy or a paper weight; any carbon containing molecule would have a well established utility as a fuel, since it can be burned; any protein would have well established utility as a protein supplement for animal food. This is not the invention of the statute.

See also MPEP at 2107-2107.02.

18) Claims 37-39, 48-52, 54 and 55 are rejected under 35 U.S.C. § 101, because the claimed invention is not supported by either a specific utility, substantial utility or a well established utility.

The asserted credible utility of the polypeptide encoded by the claimed nucleic acid or a fragment thereof is diagnostic, therapeutic and/or prophylactic. However, the claimed nucleic acid and a fragment or complement thereof, are not supported by a specific utility, because the asserted uses of the nucleic acid and a fragment or complement thereof, are not specific to *Neisseriae* in general, or to specific species of *Neisseria*. The description at lines 11-13 on page 41 of the specification states that antibodies to NGSP polypeptide of one species or strain may be used to identify and isolate the corresponding NGSP polypeptide of other *Neisseria* species or strains. The specification on pages 3 and 41 acknowledges that the polypeptide encoded by the claimed nucleic acid has about 36% homology to a non-neisserial Deg P or htrA protein of *E. coli*. The specification further states that the DNA and RNA of the invention ca be used "as probes to identify the presence of *Neisseria* in biological specimens by hybridization or PCR amplification" and "to identify **other** bacteria that might encode a polypeptide related to the *Neisseria* NGSP" [Emphasis added]. See paragraph bridging pages 34 and 35. These indicate that no *Neisseria*- or *Neisseria gonorrhoaeae*- "specific utility" existed for the polypeptide encoded by the claimed nucleic acid at the time the instant application was filed.

On page 34 and/or 35 of the instant specification, it is asserted that the polypeptides encoded by the claimed nucleic acid "may be used as ligands to detect antibodies elicited in response to *Neisseria* infections (e.g., as a diagnostic marker in diagnosing *Neisseria* infections)" and "as antigens and immunogens for inducing *Neisseria*-specific antibodies", which antibodies are "useful in immunoassays to detect *Neisseria* in biological specimens". It is asserted that the polypeptide

and/or fragments thereof "may further be used as active ingredients in vaccines to induce an immune response in an animal against *Neisseria* infections". See section 5.8 on page 34. Example 7 bears the heading, 'Efficacy of NGSP Vaccine'. Section 6.3 shows that NGSP is immunogenic and induces anti-NGSP antibodies. At section 7 of the specification, it is stated that anti-NGSP antiserum mediates complement-killing of *Neisseria*. These indicate that NGSP-induced antibodies are not specific to pathogenic *Neisseriae*. These are non-specific uses that are applicable to DNA, polypeptides or their fragments in general, but not particular or specific to the nucleic acid, polypeptide and its fragments being claimed.

One of the purposes of the invention is stated to be the use of neisserial NGSP to generate antibodies that have "diagnostic" application for identification of *Neisseria*. This is a generic and/or non-specific utility. The description at lines 11-13 on page 41 of the specification that antibodies to NGSP polypeptide of one species or strain may be used to identify and isolate the corresponding NGSP polypeptide of other *Neisseria* species or strains suggests that meningococcal and gonococcal NGSP are identical or very similar to each other and to the NGSP, for example, of non-pathogenic species of *Neisseria*. About 36% sequence identity with the Deg P protein of *E. coli* as disclosed in the second full paragraph on page 3 and in the paragraph bridging pages 41 and 42 indicates that the asserted diagnostic, therapeutic and/or prophylactic utility of non-meningococcal NGSP or the nucleic acid encoding the same, is not specific. This is of importance because the art recognizes the difficulty in developing a reliable detection, i.e., diagnostic method, for instance, to detect pathogenic species of *Neisseria*. For instance, Stern *et al.* (US 5,378,606) disclose that a "prerequisite for a **specific** therapy and control of the spread of infection is a rapid and reliable detection method for the pathogen *N. gonorrhoeae* which can be used efficiently and **specifically** detect *N. gonorrhoeae* and to **unequivocally distinguish** it from other species in particular from other members of the Neisseria genus" [Emphasis added]. See column 1, lines 43-49. Stern *et al.* teach that non-pathogenic *Neisseria* species, such as, *N. lactamica* also grow in the selective medium used for culturing pathogenic *N. gonorrhoeae,* and stress the importance of having a definitive diagnostic test (see column 1, lines 56-60). Clearly, the claimed nucleic acid and polypeptide did not have a specific utility in the diagnosis, prophylaxis or therapy of either gonococcal, meninogococcal or any other pathogenic neisserial infection at the time of filing.

Further, the claimed nucleic acid, the polypeptide and its fragments encoded by the nucleic acid are not supported by a substantial utility, because no substantial utility has been established for the claimed subject matter. It is asserted that the claimed nucleic acids, vectors comprising the same and polypeptides are "useful as reagents for clinical or medical diagnosis of *Neisseria* infections and for scientific research on the properties of pathogenicity, virulence, and infectivity of *Neisseria*, as well as host defense mechanisms". See paragraph bridging pages 34 and 35. The very need for such research indicates that the nucleic acid, the polypeptide and/or its function are not disclosed as to a currently available or substantial utility. The research contemplated to characterize a potential protein product and its biological activities does not constitute a specific and substantial utility. Identifying and studying the properties of a polypeptide itself or the mechanisms in which the polypeptide is involved does not define a "real word" context or use. These utilities are generic in nature and are applicable to a myriad of compounds. Furthermore, because the claimed invention is not supported by a specific and substantial asserted utility for the reason set forth above, credibility has not been assessed. Neither the specification as filed originally, nor any art of record discloses or suggests any property or activity for the polypeptide and fragments thereof, or nucleic acid and complements thereof, such that another non-asserted utility would be well established for the product(s) claimed. Clearly, undue experimentation would be required to attribute a "real world" utility to the claimed product.

(b) Claims 37-39, 48-52, 54 and 55 are also rejected under 35 U.S.C. § 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific utility, substantial and a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention without undue experimentation.

19) Claims 37 and 50-52 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Claims 37 and 50-52 are rejected under 35 U.S.C. § 112, first paragraph, as based on a disclosure which is not enabling. The sequence identifying number for the sequence of the Deg P protein of *E. coli,* critical or essential to the practice of the invention, but not included in the claim(s), is not enabled by the disclosure. *In re Mayhew*, 527 F.2d 1229, 188 USPQ 356 (CCPA

1976). The feature of having "about 36% sequence identity to Deg P protein of *E. coli*" is considered essential by Applicants which supposedly makes Applicants' polypeptide distinct from the polypeptide of the applied prior art. However, the SEQ ID number of the Deg P protein of *E. coli* is not reflected or recited in the claims and/or the specification. The instant specification, as originally filed, lacks adequate written description with regard to the sequence of Deg P protein of *E. coli*, the limitation of which is now included in claim 37. The nucleic acid claimed in claim 37 encodes a non-meningococcal neisserial polypeptide, about 40 KD to about 55 KD, which polypeptide has about 36% sequence identity to Deg P protein of *E. coli* when percent sequence identity is determined using a BLASTP program as recited. However, the instant specification, as originally filed, does not identify the amino acid sequence of Deg P protein of *E. coli* by a specific sequence identifier, without which one of ordinary skill in the art cannot perform the sequence comparison and practice the invention as currently claimed. Percent sequence identity can be performed only when the sequences to be compared are recited by identifying a SEQ ID number. Without such a description, undue experimentation would have been required by one of ordinary skill in the art to practice the invention as claimed.

20) Claims 48 and 54 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Many of the factors regarding undue experimentation have been summarized in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Circ. 1988) as follows:

- The quantity of experimentation necessary (time and expense);
- The amount of direction or guidance presented;
- The presence or absence of working examples of the invention;
- The nature of the invention;
- The state of the art;
- The relative skill of those in the art;
- The predictability or unpredictability of the art; and
- The breadth of the claims.

Instant claims encompass a polypeptide fragment comprising "at least 7" or "at least 8" amino acids of a polypeptide encoded by SEQ ID NO: 3, which fragment has an antigenic epitope of the polypeptide. However, the instant specification does not provide enablement for such an NGSP

polypeptide fragment comprising "at least 7" or "at least 8" consecutive or non-consecutive, contiguous or discontiguous amino acids and for a nucleotide sequence that encodes such a polypeptide fragment. The precise structural composition of the recited polypeptide fragment comprising at least 7 or 8 amino acids is not disclosed such that one of ordinary skill in the art could produce such a polypeptide fragment which contains an antigenic epitope. There is lack of disclosure as to which specific at least 7 or 8 contiguous or discontinuous amino acid residues of the polypeptide are encompassed in the recited polypeptide fragment. It is uncertain whether retention of any 7 or 8 contiguous or discontiguous amino acid residues from any part of the polypeptide encoded by the nucleotide sequence of SEQ ID NO: 3 (i.e., terminal or central parts) would yield a polypeptide fragment that would have the expected antigenic epitope along with the biologic, diagnostic or immunogenic functions preserved. It is unlikely that any linear or non-linear 7-mer or 8-mer polypeptide would retain the desired specificity, i.e., neisserial, of the recited polypeptide. It is well known that many protein epitopes are conformational and composed of discontiguous amino acid residues (see column 20, lines 55-57 of US 6,287,568). Discontiguous epitopes are formed by the three dimensional folding of a polypeptide. Without the disclosure of the specifically identified discontiguous, at least 7 or 8 amino acid residues that form the antigenic epitope, one cannot practice the instant invention without undue experimentation. The state of the art on bacterial polypeptides, for example, demonstrates the unpredictability associated with the presence of an epitope on any 10 amino acid-long fragment from any part of a given bacterial polypeptide antigen. For example, McGuinnes *et al.* (WO 90/06696) clearly demonstrate that portions of a bacterial polypeptide comprising ten contiguous amino acid residues from any random part(s) of the whole polypeptide molecule do not contain the antigenic epitope(s) that is recognized by bactericidal (protective) antibodies (see entire document, especially Figure 5). Every 10-mer portion on this bacterial polypeptide did not contain such epitope(s) indicating that the prophylactic (protective) or therapeutic efficacy of any fragment from any portion of a bacterial polypeptide antigen is not a predictable. Therefore, a 10-mer fragment from any portion of the instantly recited polypeptide encoded by the claimed nucleic acid cannot be assumed to contain or retain antigenic determinants that are needed for antigenicity, immunogenicity, or that induce prophylactic or therapeutic immune responses. Clearly, the specification does not teach polypeptide fragments comprising at least 7 or 8

amino acids of the polypeptide encoded by SEQ ID NO. 3 that contain an antigenic epitope. Since which 7-mer or 8-mer fragment would retain the antigenic specificity is neither disclosed, nor could be predicted, one of ordinary skill would be forced into experimentation that is undue. Without a disclosure of the specific amino acid residues contained within the recited polypeptide fragment encoded by the claimed nucleic acid, one of ordinary skill in the art cannot be sure of the amino acid or nucleotide sequences embraced by the claims and would not be able to make and use the nucleic acid sequence(s) as recited in the instant claims, without undue experimentation. One of ordinary skill in the art would not be able to make and use such polypeptide sequences, for example, as prophylactic, therapeutic or a diagnostic reagents, because there is no disclosure as to what amino acid residues and/or nucleotide sequences are embraced by the claims. The claims are viewed as not meeting the enablement provisions of 35 U.S.C § 112, first paragraph.

Rejection(s) under 35 U.S.C. § 112, Second Paragraph

21) Claims 37-39, 48-52 and 54 are rejected under 35 U.S.C § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

(a) Claim 37 is vague and indefinite in the recitation "polypeptide has about 36% sequence identity to Deg P protein of *E. coli* when % sequence identity is determined". The claim neither identifies the sequence of the NGSP polypeptide, nor the sequence of the Deg P protein of *E. coli* for one of skill in the art to perform the comparison, or to envisage the metes and bound of the claim. It is unclear the sequence identity of 36% is determined in comparison to what other SEQ ID number. The only comparable structural limitation of the polypeptide recited in the instant claim is the molecular weight of the NGSP polypeptide. However, one cannot use molecular weight to obtain a certain percent sequence identity. Furthermore, it is unclear whether this percent sequence identity represents continuous or discontinuous sequence identity.

(b) Claims 38 and 39 are vague in the recitation "the sequence of SEQ ID NO: 3" without reciting that the sequence is a nucleotide sequence. In order to distinctly claim the subject matter of the instant invention, it is suggested that Applicants replace the recitation with -- the nucleotide sequence of SEQ ID NO: 3--.

(c) Claim 37 is vague and indefinite in the recitation "about 36% sequence identity", because it is unclear what is encompassed in the recitation "about". Is a sequence identity of 30% or 40% included in the limitation, "about 36% sequence identity"? Furthermore, since the structural composition of a "non-cytosolic" polypeptide of any of myriad species of *Neisseria* other than *N. meningitidis* and the structural composition of "Deg P protein of *E. coli*" are not recited, the metes and bounds of the claim are indeterminate, and therefore, one of ordinary skill in the art cannot envisage the metes and bounds of the claim.

(d) Claims 48, 49 and 54 are vague in the recitation "encoded by SEQ ID NO: 3" without reciting what sequence the SEQ ID NO: 3 represents. In order to distinctly claim the subject matter of the instant invention, it is suggested that Applicants replace the recitation with --encoded by the nucleotide sequence of SEQ ID NO: 3--.

(e) Claim 50 has improper antecedence in the recitation "**the** isolated DNA of any one of claims 37, 38, 39, 48 or 49" [Emphasis added], because the claims 37, 38, 39, 48 and 49 do not recite any isolated "DNA".

(f) Claims 50-52, which depend from claim 37, is also rejected under 35 U.S.C § 112, second paragraph, as being indefinite, because of the indefiniteness or vagueness identified above in the base claim.

Rejection(s) under 35 U.S.C. § 102

22) The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> **(b)** the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

23) Claim 55 is rejected under 35 U.S.C § 102(b) as being anticipated by Halter *et al.* (*EMBO J.* 8: 2737-2744, 1989) or Pohlner *et al.* (*Nature* 325: 458-462, 1987).

Halter *et al.* teach an isolated gonococcal DNA and fragments thereof, which encode a gonococcal IgA protease and fragments thereof. The oligonucleotides are purified (see paragraph bridging pages 2743 and 2744). A polypeptide having a molecular weight of 45 kD by SDS

polyacrylamide gel electrophoresis is taught (see third paragraph, left column on page 2739; and Figure 5).

Pohlner *et al.* teach a DNA from *N. gonorrhoeae* encoding a 45 K polypeptide of an IgA protease (see page 458 and Figure 4, especially Figure 4c). Using a specific monoclonal antibody, Pohlner *et al.* detected a gonococcal 45 K protein in the outer membrane of gonococci (see page 462).

That the IgA proteases of the prior art necessarily contain a serine protease motif is inherent from the teachings of Halter *et al.* or Pohlner *et al.*

Although Halter *et al.* or Pohlner *et al.* do not refer to their polypeptide as NGSP and are silent about the use of glutamic dehydrogenase, carbonic anhydrase and myoglobin-blue as molecular weight markers as recited in the instant claim, the prior art DNA sequence is viewed as the same as the Applicants' claimed nucleic acid, and the 45 kD polypeptide encoded by the prior art DNA is viewed as the same as the instantly recited polypeptide. The Office's position that Halter's or Pohlner's DNA or the nucleotide sequence and the polypeptide encoded by the same are the same as the Applicants' nucleic acid or the nucleotide sequence and the polypeptide encoded by the same, is based upon the fact that every characteristic overlapping in Halter's or Pohlner's and Applicants' disclosure are the same. In spite of the fact that Halter *et al.* or Pohlner *et al.* do not expressly teach the use of the three molecular weight markers recited in claim 55, since the prior art nucleotide sequence and the polypeptide encoded by the same are structurally the same as the instantly claimed nucleotide sequence and the polypeptide encoded by the same, the polypeptide is expected inherently to show a molecular weight of 45 kD when glutamic dehydrogenase, carbonic anhydrase and myoglobin-blue are used as molecular weight markers in SDS gel electrophoresis. Absent evidence that the recited glutamic dehydrogenase, carbonic anhydrase and myoglobin-blue molecular weight markers change the structure of the encoded polypeptide or its molecular weight significantly, instant claim is anticipated by Halter *et al.*

Claim 55 is anticipated by Halter *et al.* or Pohlner *et al.*

Prior Art

24) The prior art made of record and not relied upon currently in any rejection is considered pertinent to Applicants' disclosure:

Plaut *et al.* (*Science* 190: 1103-1105, 1975) teach a protease enzyme of *Neisseria gonorrhoeae* which cleaves human IgA (see entire document).

- Bachovchin *et al.* (*J. Biol. Chem.* 265: 3738-3743, 1990) teach type 1 and type 2 enzymes of *Neisseria gonorrhoeae* which belong to the serine protease family of proteolytic enzymes (see entire document).

- Poulsen *et al.* (*J. Bacteriol.* 174: 2913-2921, 1992) teach the *Neisseria gonorrhoeae* type 1 and 2 IgA1 proteases are homologous serine proteases and their sequence homologies with the IgA1 protease of *H. influenzae* (see entire document). It is taught that the four *H. influenzae* type 1 *iga* genes and the *N. gonorrhoeae* type 2 gene contain conserved common regions which include the sequence VLGDSGSPLF, which site has been identified as the catalytic in the IgA1 protease of a strain of *H. influenzae* (see page 2919).

Remarks

25) Claims 37-39, 48-52 and 54 stand rejected. Claims 38 and 49 are free of prior art currently of record.

26) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center located in Crystal Mall 1. The transmission of such papers by facsimile must conform with the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The CM1 facsimile center's telephone number is (703) 308-4242, which is able to receive transmissions 24 hours a day and 7 days a week. The RightFax number for submission of before-final amendments is (703) 872-9306. The RightFax number for submission of after-final amendments is (703) 872-9307.

27) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (703) 308-9347. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 7.15 a.m. to 4.15 p.m. except one day each bi-week, which would be disclosed on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

June, 2002

SD.
S. DEVI, PH.D.
PRIMARY EXAMINER